Utility of procalcitonin in predicting mortality among cases of hospital-acquired pneumonia: a North Indian study
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Background
Data regarding the role of biomarkers like procalcitonin (PCT) in predicting treatment outcomes in hospital-acquired pneumonia (HAP) are limited in an Indian setting. We set out to determine the usefulness of PCT in predicting mortality among the cases of nosocomial pneumonia, at an 800-bed, apex tertiary care centre, in Kashmir (North India).

Patients and methods
Of the 318 confirmed cases of HAP, 60 consenting cases were selected randomly. Quantitative determination of PCT was done using immunofluorescence assays. Levels greater than 0.5 ng/ml were taken as positive. Data were collected on clinical parameters, and Acute Physiology and Chronic Health Evaluation II (APACHE-II) scores pneumonia severity index were calculated. Appropriate blood and respiratory cultures were performed.

Results
Of the 60 cases included in the study, 19 (32%) died during the hospital stay, of which 14 (74%) deaths occurred in PCT-positive cases ($P = 0.001$). The median PCT level was higher in the in-hospital mortality group (1.07 vs. 0.25), with a mean value of 1.2±2.8 vs. 1.2±2.5 in the group with no mortality ($P = 0.000$). Using multivariate analysis, positive PCT level was strongly associated with in-hospital mortality (odds ratio: 6.767, 95%CI: 1.992–22.984, $P = 0.002$) and APACHE-II score greater than 20 ($n = 14$, odds ratio=4.5, 95%CI=1.448–13.984, $P = 0.009$). Using receiver operating characteristic analysis, PCT had apropos discrimination power for in-hospital mortality (0.713 of area under the curve) and higher APACHE-II scores (0.753 of area under the curve). Using Cox regression model for mortality in PCT-positive group, the calculated hazard ratio was 3.273 (95%CI: 1.076–9.951, $P = 0.037$).

Conclusion
PCT might have a vital role in the management of HAP, as a predictor of the poor treatment outcome.

Keywords: \textit{Acinetobacter baumannii}, bacterial, enterobacteriaceae, pneumonia, pneumonia, procalcitonin, respiratory tract infections

Introduction
Hospital-acquired pneumonia (HAP) is the most common life-threatening hospital-acquired infection, and most cases are associated with mechanical ventilation. Moreover, it is associated with significant increases in length of hospital stay, mortality and costs [1]. To prevent irrational overuse of antibiotics, the role of biomarkers like procalcitonin (PCT) and C-reactive protein was suggested to estimate the presence of sepsis and response to antibiotics [2,3]. PCT was described as a marker of sepsis in 1993 [4]. The induction of PCT is more strictly regulated as compared with cytokines: there is no significant PCT production in stimulated whole blood, but PCT production has been observed in various tissues during sepsis. The induction of circulating PCT is related to the activation and adherence of monocyct cells, which occur during sepsis as well as in other conditions such as after tissue trauma [5]. Varieties of human tissues express PCT-I, PCT-II and calcitonin gene-related peptide-I mRNAs, with highest levels detected in liver, testis, lung, prostate, kidney and small intestine, differing in the proportions of expression [6]. However, the recent American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA) guidelines

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have not recommended PCT testing for diagnostic purposes, and the role of biomarkers in the management of HAP has become almost obsolete. Among all the biomarkers, the only biomarker to have any part is PCT in combination with clinical criteria, in determining the length of treatment [7]. Moreover, there is a growing body of evidence for nondiagnostic uses of PCT, especially in predicting an adverse treatment outcome [8,9]. This study was designed to determine if PCT can predict mortality in patients with HAP [including healthcare-associated pneumonia (HCAP)] requiring hospitalisation in Kashmir.

**Patients and methods**

**Study design**

In this single-centre, prospective observational study, 60 cases of HAP were randomly (software generated) selected from 318 patients seen over a 2-year period from September 2013 to September 2015 (Figs 1 and 2).

**Figure 1**

Flow diagram of patients included in the study – subsets indicating in-hospital mortality in each group. ATS/IDSA, American Thoracic Society/Infectious Diseases Society of America; CAP, community-acquired pneumonia; HAP, hospital-acquired pneumonia; HCAP, healthcare-associated pneumonia; PCT, procalcitonin.

**Figure 2**

Microbiological results and relation to procalcitonin. HAP, hospital-acquired pneumonia; HCAP, healthcare-associated pneumonia.
Paediatric and immunocompromised patients were excluded from the study. Patients were diagnosed as a case of HAP (including HCAP) based on ATS/IDSA guidelines, 2005 [10]. Quantitative determination of PCT was done using fluorescence immunoassay, as per manufacturer’s instruction (Boditech Med Inc., Gang-Won-Do, South Korea). Values less than 0.5 ng/ml were considered negative. Sputum and endotracheal aspirate (ETA) cultures were done using blood agar, MacConkey agar and Chocolate agar. BacT/Alert 3D (BioMérieux, Inc., North Carolina, USA) automated system was used for blood cultures. The threshold value of 10^5 colony-forming units/ml was used, for ETA cultures, and values below the threshold were considered as colonisations [11]. Antibiotic susceptibility testing for isolates from sputum and ETA was done by Kirby and Bauer disc diffusion method as per Clinical Laboratory Standard Institute guidelines. Antibiotic susceptibility testing of isolates from blood was done on VITEK 2 (BioMérieux, Inc., North Carolina, USA). Data were collected for demographics and co-morbidities and were recorded in a predefined proforma. Multidrug resistant (MDR) pathogen risk factors, baseline performance (Charlson comorbidity index) [12], severity of pneumonia [pneumonia severity index (PSI) score and Acute Physiology and Chronic Health Evaluation II (APACHE-II) score], blood culture and respiratory culture results (sputum and ETA), clinical outcomes, and in-hospital mortality were recorded.

**Statistical analysis**

Discrete variables are expressed as counts (percentage), and continuous variables as mean±SD. Student’s t-test (parametric) and the Mann–Whitney (nonparametric) test were used to assess significant differences in quantitative variables. For qualitative variables, Pearson’s χ²-test or Fisher’s exact test for tables (2×2) was used. The receiver operating characteristic (ROC) curve was used for testing a test variable to differentiate between two groups. Multinominal regression analysis was used to determine various factors predicting mortality. All data were analysed using 95%CI, and P value less than 0.05 was considered significant. Data were analysed using SPSS software (16.0; SPSS Inc., Chicago, Illinois, USA).

**Ethics**

The Institute Ethics Committee approved the study.

**Results**

The 60 patients included 36 male and 24 females, with age ranging from 17 to 90 years (mean: 57.10±17.8 years). Of the 60 cases, 15 cases aged less than or equal to 45 years, 17 cases between 46 to 60 years of age, and 28 cases greater than 60 years. Thirty-three (55%) cases were current smokers. Cases included in the study were critically ill, and 35 cases had Charlson comorbidity index scores greater than 3, with more co-morbidities in HCAP (n=20) than HAP (n=15). Details of various patient characteristics, co-morbidities along with MDR pathogen risk factors among PCT-positive and PCT-negative groups are shown in Table 1a. Table 1b depicts the comparison between HCAP and HAP groups, separately. Twenty-nine patients had positive PCT levels. The mean age of cases in PCT-positive group was 54.73±19.2 (vs. 58.91±16.6) years. The mean PCT value was 1.5247±2.58231. Among the PCT-positive group, the mean PCT value of 3.1765±3.27525 was seen vs. 0.2615±0.04 in the PCT-negative group.

**Clinical and baseline features**

The cases included in the study were critically ill, with a mean APACHE-II score of 19±8.364, with PCT-positive cases having a mean APACHE-II score of 22.58±9.407, which was higher than the mean APACHE-II score (16.38±6.396) in PCT-negative cases. The mean PSI score of 124.52±50.497 was seen among the 60 cases, with PCT-positive cases showing mean PSI of 133.31±51.387, which was higher than the value of mean PSI score in PCT-negative cases (117.79±49.508). A total of 25 cases were in PSI class V. Moreover, 28 cases had consolidation (n=22) and multilobar infiltrates (n=6). Among the cases with positive PCT levels, eight cases had consolidation, and three had multilobar infiltrates. Fifteen cases developed coagulopathy (INR>1.5, or aPTT >60 s), and 26 cases developed worsening of renal functions [increase in serum Cr≥0.3 mg/dl (26.5 µmol/l) within 48 h or an increase in SCR to greater than 1.5 times baseline, which is known or presumed to have occurred within the previous 7 days or a urine volume of <0.5 ml/kg/h for 6 h] [13]. Septic shock (mean arterial pressure≤70 mmHg) was seen in 23 cases. Thirty-six cases had the length of stay below 14 days, out of which 13 cases were PCT positive.

**Microbiological results**

A total of 25 (41.7%) cases had positive cultures, of which 18 (72%) were associated with positive PCT levels (P=0.000). Positive respiratory cultures were obtained from 14 (23%) cases, of which 13 (93%) were positive for PCT (P=0.000). Blood cultures were positive from 16 (27%) cases, of which 10 (63%) cases were PCT positive (P=0.071; Table 2).
Acinetobacter baumannii was the most frequently isolated (n=10, 17%) followed by Escherichia coli (n=7, 12%) and Klebsiella pneumoniae (n=6, 10%). Most of the Acinetobacter baumannii and E. coli were isolated from cases of HAP (n=7, 12%) and HCAP (n=6, 10%), respectively. Collectively, bacteria belonging to Enterobacteriaceae (n=12, 20%) and ‘ESCAPE bugs’ (n=21, 35%) as groups were related to positive PCT levels (ESCAPE: Enterococcus faecium, Staphylococcus aureus, Clostridium difficile, Acinetobacter baumannii, Pseudomonas aeruginosa and Enterobacteriaceae family; the group of bacteria with an ability to ‘escape’ the effect of antibiotics, by developing resistance) [14].

### Table 1 Baseline demographics

<table>
<thead>
<tr>
<th>Co-morbidities</th>
<th>HCAP (n=35) [n (%)]</th>
<th>HAP (n=25) [n (%)]</th>
<th>P value</th>
<th>PCT positive (n=26) [n (%)]</th>
<th>PCT negative (n=34) [n (%)]</th>
<th>P value</th>
<th>Total (n=60) [n (%)]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>≤ 45 years</td>
<td>8 (23)</td>
<td>7 (28)</td>
<td>0.650</td>
<td>10 (42)</td>
<td>5 (14)</td>
<td>0.035</td>
<td>15 (25)</td>
</tr>
<tr>
<td>46–60 years</td>
<td>10 (29)</td>
<td>7 (28)</td>
<td>0.961</td>
<td>5 (21)</td>
<td>12 (33)</td>
<td>0.171</td>
<td>17 (28)</td>
</tr>
<tr>
<td>&gt;60 years</td>
<td>17 (49)</td>
<td>11 (44)</td>
<td>0.726</td>
<td>11 (46)</td>
<td>17 (47)</td>
<td>0.554</td>
<td>28 (47)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>20 (57)</td>
<td>16 (64)</td>
<td>0.593</td>
<td>19 (79)</td>
<td>17 (47)</td>
<td>0.071</td>
<td>36 (60)</td>
</tr>
<tr>
<td><strong>Co-morbidities</strong></td>
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<td></td>
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</tr>
<tr>
<td>Hypertension</td>
<td>32 (53)</td>
<td>21 (84)</td>
<td>0.377</td>
<td>20 (83)</td>
<td>33 (92)</td>
<td>0.016</td>
<td>53 (88)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>6 (17)</td>
<td>3 (12)</td>
<td>0.582</td>
<td>2 (8)</td>
<td>7 (19)</td>
<td>0.166</td>
<td>9 (15)</td>
</tr>
<tr>
<td>Chronic lung condition</td>
<td>14 (40)</td>
<td>6 (24)</td>
<td>0.195</td>
<td>5 (21)</td>
<td>15 (42)</td>
<td>0.043</td>
<td>20 (33)</td>
</tr>
<tr>
<td>COPD</td>
<td>11 (31)</td>
<td>5 (20)</td>
<td>0.324</td>
<td>5 (21)</td>
<td>11 (31)</td>
<td>0.255</td>
<td>16 (27)</td>
</tr>
<tr>
<td>Asthma</td>
<td>1 (3)</td>
<td>1 (4)</td>
<td>0.808</td>
<td>0</td>
<td>2 (6)</td>
<td>0.208</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Interstitial lung disease</td>
<td>1 (3)</td>
<td>0</td>
<td>0.394</td>
<td>0</td>
<td>1 (3)</td>
<td>0.378</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>1 (3)</td>
<td>1 (4)</td>
<td>0.808</td>
<td>0</td>
<td>2 (6)</td>
<td>0.208</td>
<td>2 (3)</td>
</tr>
<tr>
<td>CKD</td>
<td>4 (11)</td>
<td>1 (4)</td>
<td>0.305</td>
<td>2 (8)</td>
<td>3 (8)</td>
<td>0.875</td>
<td>5 (8)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>8 (23)</td>
<td>9 (36)</td>
<td>0.265</td>
<td>9 (38)</td>
<td>8 (22)</td>
<td>0.345</td>
<td>17 (28)</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>4 (11)</td>
<td>4 (16)</td>
<td>0.608</td>
<td>4 (17)</td>
<td>4 (11)</td>
<td>0.683</td>
<td>8 (13)</td>
</tr>
<tr>
<td>Charlson comorbidity index score &gt;3</td>
<td>20 (57)</td>
<td>15 (60)</td>
<td>0.825</td>
<td>16 (67)</td>
<td>19 (53)</td>
<td>0.660</td>
<td>35 (58)</td>
</tr>
<tr>
<td><strong>Other patient factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trauma/emergency surgery</td>
<td>0</td>
<td>2 (8)</td>
<td>0.089</td>
<td>2 (8)</td>
<td>0</td>
<td>0.100</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>19 (54)</td>
<td>14 (56)</td>
<td>0.295</td>
<td>14 (58)</td>
<td>19 (53)</td>
<td>0.452</td>
<td>33 (55)</td>
</tr>
<tr>
<td>Former smoker</td>
<td>4 (11)</td>
<td>6 (24)</td>
<td>0.295</td>
<td>6 (25)</td>
<td>4 (11)</td>
<td>0.452</td>
<td>10 (17)</td>
</tr>
<tr>
<td>Never smoker</td>
<td>12 (34)</td>
<td>5 (20)</td>
<td>0.295</td>
<td>6 (25)</td>
<td>11 (31)</td>
<td>0.452</td>
<td>17 (28)</td>
</tr>
<tr>
<td><strong>MDR risk factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemodialysis</td>
<td>1 (11)</td>
<td>4 (14)</td>
<td>0.305</td>
<td>2 (8)</td>
<td>3 (8)</td>
<td>0.875</td>
<td>5 (8)</td>
</tr>
<tr>
<td>Inhaled steroid</td>
<td>5 (17)</td>
<td>3 (12)</td>
<td>0.582</td>
<td>5 (21)</td>
<td>4 (11)</td>
<td>0.422</td>
<td>9 (15)</td>
</tr>
<tr>
<td>Systemic steroids</td>
<td>4 (11)</td>
<td>0</td>
<td>0.080</td>
<td>4 (17)</td>
<td>0</td>
<td>0.070</td>
<td>4 (7)</td>
</tr>
<tr>
<td>Home wound care</td>
<td>2 (6)</td>
<td>0</td>
<td>0.224</td>
<td>0</td>
<td>2 (6)</td>
<td>0.208</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Antibiotic use in last 3 months (HCAP) or before onset of pneumonia (HAP)</td>
<td>34 (97)</td>
<td>2 (8)</td>
<td>0.000</td>
<td>18 (75)</td>
<td>23 (64)</td>
<td>0.896</td>
<td>41 (68)</td>
</tr>
<tr>
<td>Previous hospitalisation in the last 3 months</td>
<td>31 (89)</td>
<td>1 (4)</td>
<td>0.000</td>
<td>11 (46)</td>
<td>21 (58)</td>
<td>0.134</td>
<td>32 (53)</td>
</tr>
</tbody>
</table>

CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; HAP, hospital-acquired pneumonia; HCAP, healthcare-associated pneumonia; PCT, procalcitonin.

### Table 2 Sensitivity and specificity of procalcitonin as a marker in relation to culture results, at the cut-off value of 0·5 ng/ml

<table>
<thead>
<tr>
<th>Specimen文化 result</th>
<th>Sensitivity [95%CI (upper limit–lower limit)]</th>
<th>Specificity [95%CI (upper limit–lower limit)]</th>
<th>PPV [95%CI (upper limit–lower limit)]</th>
<th>NPV [95%CI (upper limit–lower limit)]</th>
<th>P-LR [95%CI (upper limit–lower limit)]</th>
<th>N-LR [95%CI (upper limit–lower limit)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive culture</td>
<td>72 (50.40–87.13)</td>
<td>77.14 (59.45–88.96)</td>
<td>69.23 (48.10–84.91)</td>
<td>79.41 (61.59–90.66)</td>
<td>3.15 (1.63–6.07)</td>
<td>0.36 (0.19–0.69)</td>
</tr>
<tr>
<td>Positive blood culture</td>
<td>62.5 (35.9–83.7)</td>
<td>82.4 (64.8–92.6)</td>
<td>62.5 (35.9–83.7)</td>
<td>82.4 (64.8–92.6)</td>
<td>3.54 (1.56–8.04)</td>
<td>0.46 (0.24–0.87)</td>
</tr>
<tr>
<td>Positive lower respiratory tract specimen culture</td>
<td>92.9 (64.2–99.6)</td>
<td>71.7 (56.3–83.5%)</td>
<td>92.9 (64.2–99.6)</td>
<td>97.1 (82.9–99.8)</td>
<td>3.26 (2.03–5.32)</td>
<td>0.10 (0.01–0.67)</td>
</tr>
</tbody>
</table>
Seven (12%) cases had a polymicrobial aetiology (HCAP: 2, 29%; HAP: 5, 71%) (Fig. 3).

Treatment outcome

Nineteen (32%) patients died during the hospital stay, and 14 (23%) deaths were observed in PCT-positive group [vs. five (8%) deaths in PCT-negative group; Table 3].

On multivariate analysis, positive PCT levels were related to death, septic shock, coagulopathy, arterial hypoxaemia (PaO₂/FiO₂ < 300), and APACHE-II score greater than 20.

Among cases with positive respiratory cultures, six (43%) cases died (P=0.304), whereas in cases with positive blood cultures, eight (50%) cases died (P=0.066), in the hospital. Overall, the in-hospital mortality was higher in cases with positive culture results (n=12, 63%), versus seven (12%) in those without positive cultures (P=0.02). The mortality was significantly higher in HAP group (n=11, 58%; P=0.083) than in HCAP group (n=8, 42%). Mortality was nearly three times higher among those with a positive PCT level (n=14, 74%) compared with those with a negative PCT (P=0.001). The various risk factors identified as predictors of in-hospital mortality are depicted in Table 4. Using ROC curve, PCT showed a sensitivity of 78.9% and a specificity of 34.1% and area under the curve (AUC) of 0.713 (P=0.008). Other significant variables were PSI class and APACHE-II score. Leucocyte count greater than 12 000/mm³ also showed the sensitivity of 94.7% and specificity of 82.9% (Fig. 3). PCT levels were positive in 26 (43%) cases [HCAP: n=12 (46%); HAP: n=14 (54%); P=0.094]. PCT was found to be 72% sensitive and 77% specific for positive culture results (details in Table 5). The median PCT level was higher in the in-hospital mortality group (1.07 vs. 0.25), with a mean value of 1.2±2.8 (vs. 1.2±2.5).

Using Cox regression analysis model, for positive PCT positive group, the hazard ratio (HR) calculated was 3.273 (95%CI: 1.076–9.951; P=0.037), and hence the mortality in this group was significantly greater than PCT-negative group. Mortality was also considerably high among patients with APACHE-II scores greater than or equal to 17 (HR: 2.692; 95%CI: 1.015–7.144; P=0.047), septic shock (HR: 2.433; 95%CI: 0.973–6.085; P=0.057), and PSI Class IV and higher (HR: 5.318; 95%CI: 1.206–23.452; P=0.027).

Discussion

The demographic data, in our study, are consistent with previously published studies, and most of the patients were male and greater than 60 years of age [2,8]. Most of the patients had significant co-morbidities, including, respiratory, cardiovascular, renal and neurological co-morbidities. Overall, the mortality rate of patients is relatively high at 32%. All the patients needed hospitalisation in ICU or high-dependency units. The risk factors for MDR pathogen infections, a higher rate of infection with multidrug or extensively antibiotic-resistant pathogens, significant co-morbidities, and higher APACHE-II
Scores, all contributed to higher mortality rates in the study group. Among PCT-positive cases, the mortality was almost three times higher ($P=0.001$), with higher median PCT level (1.07 vs. 0.25). ROC analysis also showed a significant role of PCT in predicting in-hospital mortality in cases of HAP (AUC±SE=0.713±0.071; 95%CI: 0.574–0.852; $P=0.008$). Using multivariate analysis, the relation of PCT (0.5 ng/ml) to predict mortality in cases of HAP was established (odds ratio: 6.767; 95%CI: 1.992–22.984; $P=0.002$).

The utility of PCT in predicting adverse treatment outcome has been well studied in CAP [15–26].
All of these studies varied in selecting the PCT cut-off level for use as prognostic indicator, ranging from 0.1 ng/ml [19,21,25] to 5 ng/ml [25] and 21.91 ng/ml [16]. The studies determined sensitivity and specificity of PCT in predicting mortality in patients with CAP, ranging from 56/90.9 at a cut-off of 0.5 [18] to 82/75 at a cut-off level of 1.5 [26]. In a meta-analysis done by Liu et al. [27], the pooled sensitivity and specificity of PCT in predicting mortality in CAP was found to be 0.69 (95%CI: 0.57–0.79) and 0.74 (95%CI: 0.60–0.84). Besides CAP, the role of PCT in predicting mortality in pneumonia has been well studied in VAP [28–36]. In the meta-analysis done by Liu et al. [27], the pooled sensitivity and specificity of PCT in predicting mortality in CAP was found to be 0.80 (95%CI: 0.75–0.85) and 0.74 (95%CI: 0.63–0.82).

However, very few studies have reported utility of PCT in predicting adverse clinical outcome in HAP [35] and HCAP group of pneumonia. Bloos et al. [37] conducted a study in cases of CAP, HCAP and VAP and found PCT as a fair predictor of 28-day mortality, at cut-off level of 1.1, with odds ratio of 7 (95%CI 2.6–25.2).

The recently published studies have explored the use of PCT, mainly in CAP, but in the most recently published study, Hong et al. [9], in the first study to evaluate PCT as a predictor of outcomes in patients with HCAP, concluded that high PCT on admission was strongly associated with ICU admission and 30-day mortality. The mortality rate in this study was 18%, with higher median PCT levels in 30-day mortality group (3.3 vs. 0.4 ng/ml; P<0.001), and on multivariate analysis, high PCT (>2.0 ng/ml) was strongly associated with 30-day mortality (HR: 2.25; 95%CI: 1.25–5.340; P=0.035). The ROC analysis of PCT had an excellent discrimination power regarding 30-day mortality in patients with HCAP (0.768 of the AUC). The relatively lower median PCT levels in our study can be explained by prior antibiotic use, before hospitalisation (HCAP). Andrijevic et al. [17], in a recently published study, found PCT to be useful in predicting mortality in cases of community-acquired pneumonia. ROC curve analysis confirmed significant role of PCT as a mortality predictor in patients with CAP (AUC±SE=0.667±0.062; 95%CI: 0.546–0.789; P=0.012), and as a predictor of mortality at the cut-off value of 2.56 ng/ml, PCT showed sensitivity of 76% and specificity of 61.8%. Kasamatsu et al. [8], in a similar study in patients with CAP, found 30-day mortality among patients with higher PCT (>0.5 ng/ml) was significantly higher (12%). The ROC analysis for prediction of survival, for PCT, was 0.80 of the AUC. Hence, it is evident that the positive procalcitonin levels can be an independent predicting factor for in-hospital mortality, in HCAP and HAP.

In the setup of developing nations, the PCT can still be useful, despite the irrational overuse of antibiotics, prescription or nonprescription [38]. We also found that despite antibiotic intake, the marker proved to be an essential predictor of in-hospital mortality in the HAP.

In a large, most recent (May 2017) multicentre, blinded, prospective observational clinical trial – Multicentre Procalcitonin Monitoring Sepsis (MOSES) study [39] – it was found that inability to decrease PCT by more than 80% is a significant independent predictor of mortality and may aid in sepsis care. The primary end point of this study was 28-day all-cause mortality. The data from 107 nonsurvivors and 539 survivors were analysed. Among the nonsurvivors, confirmed infection was found in 88 (82%) of cases, with initial PCT (>0.5 ng/ml) strongly associated with mortality (HR: 2.254; 95%CI: 1.250–5.340; P=0.035). The emphasis was on PCT kinetics from baseline to the

| Table 5 Multivariate analysis of factors predicting in-hospital mortality |
|---------------------------------|--------|--------|-------------|--------|
| Death                          | P value | Odds ratio | 95% confidence interval |
|                                |        |          | Lower bound | Upper bound |
| PSI class V                    | 0.054  | 6.135    | 0.969       | 38.856    |
| Arterial hypoxaemia            | 0.887  | 1.125    | 0.221       | 5.734     |
| MAP <65 mmHg                   | 0.023  | 3.750    | 1.196       | 11.762    |
| MAP <70 mmHg                   | 0.038  | 3.323    | 1.071       | 10.310    |
| Procalcitonin >0.5 ng/ml       | 0.002  | 6.767    | 1.992       | 22.984    |
| Acinetobacter baumannii        | 0.341  | 2.364    | 0.402       | 13.891    |
| ESCAPE bacteria                | 0.092  | 3.625    | 0.810       | 16.220    |
| Chronic lung disease           | 0.030  | 0.112    | 0.016       | 0.806     |

MAP, mean arterial pressure; PSI, pneumonia severity index.
value on day 4, with a decrease of greater than 80% seen in 23 (22%), where the decrease in PCT kinetics was less than or equal to 80%. Prognostic measures at these cut-offs showed a sensitivity of 77% (95%CI: 69–85%) with a specificity of 39% (95%CI: 36–43%). Mortality was also found to be higher in patients still hospitalised in ICU at day 4 (26%). Among patients discharged from the ICU by day 4 who had a high baseline PCT value of greater than 2 μg/l, mortality was more than threefold increased if PCT did not decrease by greater than 80% (19 vs. 5%). For patients in ICU at day 4, with low baseline PCT of less than 2 μg/l, mortality was about threefold higher if PCT did not decrease by greater than 80% compared with PCT that decreased by greater than 80% (26 vs. 10%) [39].

The year 2016, ATS/IDSA guidelines have not included PCT in management, but in the tailoring of antibiotic treatment, that too in combination with clinical features. Moreover, the meta-analysis of three randomised control trials [40–42], by ATS/IDSA panel, which specifically evaluated the discontinuation of antibiotic therapy for VAP on the basis of PCT levels plus clinical criteria versus clinical criteria alone, found that former group had a shorter duration of antibiotic therapy (9.1 vs. 12.1 days; P<0.00001, but no difference in mortality). Other outcomes included no effects on the duration of mechanical ventilation, length of ICU stay, length of hospital stay, the incidence of recurrent pneumonia, or development of resistance [7].

As already discussed, expression of PCT-I, PCT-II and CGRP-1 mRNAs is high in lungs, only after liver and testis [3]. Our study results also showed higher sensitivity and specificity of PCT to positive respiratory cultures, than to positive blood cultures. Owing to small sample size, we could not get a statistically significant relationship between positive respiratory tract specimen culture and mortality, but the relationship of positive PCT levels was substantial to positive blood cultures. The high microbiological yield in the study group (42%) is another critical factor, which is more than the overall rate of pathogen detection among patients with CAP (30–40%) [43]. Among the scoring systems, in case of nosocomial pneumonia, the APACHE score showed better utility in predicting mortality, compared with the PSI score. Hence, it can be concluded that PCT not only is a sensitive marker for bacterial infections, and has a significant role in the tailoring of antibiotics, but also has more sensitivity for respiratory tract infections, in specific. Hence, the use of PCT in the management of respiratory tract infections is plausible. Moreover, PCT has strong relation with coagulopathy, septic shock and mortality and can be used to predict the severity of illness (like or alongside APACHE-II scores), mortality in cases of HAP, and might be helpful in making decisions for patient management in intensive care units.

Limitations
This is a single-centre study and the sample size is small.

Conclusion
The use of PCT in the management of HAP, although PCT is no more recommended in diagnostic part, is an excellent predictor of disease severity and adverse treatment outcomes among patients with HAP, in our setting.

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